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SMC2156

durvalumab 50mg/mL concentrate for solution for infusion (Imfinzi®)

AstraZeneca

10 May 2019

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission considered under the ultra-orphan and end of life process

durvalumab (Imfinzi®) is accepted for use within NHSScotland.

Indication under review: as monotherapy for the treatment of locally advanced, unresectable non-small cell lung cancer (NSCLC) in adults whose tumours express PD-L1 [programmed cell death ligand 1] on ≥1% of tumour cells and whose disease has not progressed following platinum-based chemoradiation therapy.

Durvalumab, compared with placebo, improved progression-free survival and overall survival in adults who have locally advanced unresectable NSCLC with PD-L1 expressed on ≥1% of tumour cells and disease that has not progressed following platinum-based chemoradiation therapy.

This SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of durvalumab. This advice is contingent upon the continuing availability of the PAS in NHSScotland or a list price that is equivalent or lower.

This advice takes account of views from a Patient and Clinician Engagement (PACE) meeting.

Chairman
Scottish Medicines Consortium

Indication

As monotherapy for the treatment of locally advanced, unresectable non-small cell lung cancer (NSCLC) in adults whose tumours express PD-L1 [programmed cell death ligand 1] on ≥ 1% of tumour cells and whose disease has not progressed following platinum-based chemoradiation therapy.[1]

Dosing Information

Durvalumab 10mg/kg intravenous (IV) infusion over 60 minutes every 2 weeks, until disease progression or unacceptable toxicity, or a maximum of 12 months. It is recommended to continue treatment for clinically stable patients with initial evidence of disease progression until disease progression is confirmed.

Dose escalation or reduction is not recommended. Dose withholding or discontinuation may be required to manage adverse events as detailed in the summary of product characteristics.

Patients with locally advanced NSCLC should be evaluated for treatment based on the tumour expression of PD-L1 confirmed by a validated test. Treatment must be initiated and supervised by a physician experienced in the treatment of cancer.[1]

Product availability date

24 September 2018

Durvalumab meets SMC ultra-orphan and end-of-life criteria for this indication.

Background

Durvalumab is an inhibitor of programmed cell death ligand-1 (PD-L1), which is a protein that helps tumours evade detection and elimination by the immune system. By inhibiting PD-L1 durvalumab enhances anti-tumour immune responses and increases T-cell activation. It is licensed for up to 12 months maintenance treatment in adults with locally advanced, unresectable (stage III) NSCLC with PD-L1 expressed on ≥1% of tumour cells and disease that has not progressed after platinum-based chemoradiation therapy.[1]

Durvalumab for use in this indication has been considered by SMC using its decision-making framework for the assessment of ultra-orphan medicines.

Nature of condition

Durvalumab is the first PD-L1 inhibitor licensed for the treatment of stage III (unresectable locally advanced) NSCLC that has not progressed after standard first-line treatment with

platinum-based chemoradiotherapy.[1] It meets SMC ultra-orphan and end-of-life criteria for this indication.

Unresectable locally advanced NSCLC is treated with concurrent platinum-based chemotherapy plus radical radiotherapy (chemoradiotherapy). If concurrent treatment is not possible, sequential chemotherapy then radiotherapy is recommended. Guidelines from the European Society of Medical Oncology (ESMO) in 2017, the Scottish Intercollegiate Guidelines Network (SIGN) in 2014, the National Institute for Health and Care Excellence (NICE) in 2011 and the British Thoracic Society (BTS) in 2010 do not recommend any further treatment after concurrent or sequential chemotherapy plus radiotherapy, although patients should have regular follow-up.[2-5]

Clinical experts consulted by SMC advised that currently patients have clinical follow-up without any active maintenance therapy. They noted the low cure rates in patients with stage III NSCLC treated with chemoradiotherapy and highlighted an unmet need for further effective therapies.

A patient and clinician engagement (PACE) meeting was held to consider the added value of durvalumab in the context of treatments currently available in NHSScotland. At the PACE meeting, attention was drawn to the poor prognosis, with a 5 year survival of 15 to 30%, in patients with locally advanced (stage III) NSCLC. It was also highlighted that following chemoradiation therapy, patients are currently not given active treatment but are monitored for signs of disease progression. There is an unmet need for effective treatments to improve the long-term survival of these patients.

Impact of new technology

Summary of evidence on comparative efficacy

A double-blind phase III study (PACIFIC) recruited adults with unresectable locally advanced stage III NSCLC that had not progressed after at least two cycles of platinum-based chemotherapy in combination with definitive radiotherapy with last dose of radiation no more than 42 days before randomisation. Patients had World Health Organisation performance status 0 or 1. They were randomised, with stratification for age (<65 versus ≥65 years), sex and smoking history (current or former versus never), in a 2:1 ratio to IV infusion of durvalumab 10mg/kg or placebo every two weeks until disease progression, initiation of other anti-cancer treatment, unacceptable toxicity or to the maximum of 12 months. The co-primary outcomes were progression-free survival (PFS) according to response evaluation criteria in solid tumours (RECIST) version 1.1 assessed by a blinded independent review panel and overall survival. These were assessed in all randomised patients.[6,7]

At the first interim analysis of PFS at data cut-off 13 February 2017 (median follow-up 14.5 months) and at an updated analysis at data cut-off 22 March 2018 (median follow-up 25.2 months) PFS was significantly greater with durvalumab compared with placebo in the total study population and the subgroup with PD-L1 on ≥1% of tumour cells, which is representative of the indication. At the first interim analysis of overall survival at data cut-off 22 March 2018 an independent data and safety monitoring committee concluded that the pre-specified criteria for unblinding (p-value crossed the efficacy boundary of 0.00274) had been fulfilled and a significant benefit in overall survival was observed with durvalumab compared with placebo in the total study population and PD-L1 ≥1% subgroup. The key secondary outcome, objective response rate (complete or partial response on RECIST version 1.1) was significantly improved with durvalumab compared with placebo in both populations. These results are detailed in table 1.[6-9]

Table 1: Primary and key secondary outcomes of PACIFIC study.[6-9]

		Total study population		PD-L1≥1% subgroup	
		Durvalumab	**Placebo**	**Durvalumab**	**Placebo**
Progression-free survival by blinded independent review					
Cut-off 13.2.17	Events	45% (214/476)	66% (157/237)	40% (84/212)	65% (59/91)
	Median (months)	16.8	5.6	17.8	5.6
	HR (95% CI)	0.52 (0.42 to 0.65), p<0.001		0.46 (0.33 to 0.64)	
Cut-off 22.3.18	Events	51% (243/476)	73% (173/237)	47% (99/212)	72% (66/91)
	Median (months)	17.2	5.6	23.9	5.6
	HR (95% CI)	0.51 (0.41 to 0.63), p<0.0001		0.44 (0.31 to 0.63)	
Overall survival					
Cut-off 22.3.18	Events	38% (183/476)	49% (116/237)	33% (70/212)	50% (45/91)
	Median (months)	NR	28.7	NR	29.1
	HR (95% CI)	0.68 (0.53 to 0.88), p=0.003		0.53 (0.36 to 0.77)	
Objective response rate by blinded independent review					
13.2.17	Events	28% (126/443)	16% (34/213)		
22.3.18	Events	30% (133/443)	18% (38/213)	32% (64/197)	16% (14/85)

PD-L1≥1% = programmed cell death ligand-1 on ≥1% of tumour cells; HR (95% CI) = hazard ratio (95% confidence interval); NR = not reached. Objective response = complete or partial response on response evaluation criteria in solid tumours (RECIST) version 1.1.

European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 items (EORTC QLQ-C30) and lung cancer module (EORTC QLQ-LC13) indicated that there were no differences between durvalumab and placebo groups in patient reported symptoms, function and health-related quality-of-life at baseline and no clinically meaningful differences (as defined by a difference of greater than or equal to 10 points) through to week 48.[6]

Summary of evidence on comparative safety

The European Medicines Agency (EMA) review concluded that the safety profile of durvalumab was as expected for a PD-L1 inhibitor and was in line with other medicines in this class.[6]

In the PACIFIC study at the data cut-off 31 July 2017 within the durvalumab and placebo groups 97% (460/475) and 95% (222/234) of patients had an adverse event, which were grade 3 or 4 in 32% and 28%, serious in 29% and 23% and led to study treatment discontinuation in 15% and 9.8%, respectively. Treatment-related adverse events were reported more often in the durvalumab group, compared with placebo (68% and 53%), which were grade 3 or 4 in 12% and 4.7%, serious in 8.4% and 3.4% and led to study treatment discontinuation in 9.9% and 3.4%, respectively.[6]

The majority of adverse events were reported in the first three months of the study and the main differences in frequencies between the groups were mostly accounted for by known risks of PD-L1 inhibitors, for example immune-related events, such as pneumonitis, and infections. At the 31 July 2017 cut-off within the durvalumab and placebo groups the following adverse events were reported: radiation pneumonitis (20% and 15%), pneumonitis (13% and 7.7%), pneumonia (13% and 7.7%), upper respiratory tract infection (12% and 9.8%), nasopharyngitis (8.6% and 6.0%), cough (35% and 25%), fatigue (24% and 20%), dyspnoea (22% and 24%), and pyrexia (15% and 9.0%). Other adverse events more commonly reported in the durvalumab group than in the placebo group included pruritus (12% and 4.7%), rash (12% and 7.3%), hypothyroidism (12% and 1.7%), and hyperthyroidism (7.4% and 1.7%). The most common serious adverse events within the durvalumab and placebo groups were pneumonia (5.7% and 5.1%), pneumonitis (3.4% and 3.0%), radiation pneumonitis (3.6% and 1.3%), lung infection (1.3% and 0.9%) and chronic obstructive pulmonary disease (1.1% and 0%), respectively.[6]

Summary of clinical effectiveness issues

In the PACIFIC study in the total study population and the subgroup with PD-L1 ≥1%, representative of the indication, PFS was improved by about 11 and 12 months, respectively, compared with placebo. The latest overall survival analysis (22 March 2018) data were immature. They indicate significant improvement in overall survival with durvalumab compared with placebo in both the total study population and PD-L1 ≥1%

subgroup, with a hazard ratio of 0.53 in the latter. The EMA considers these results to be clinically relevant in a population at high risk of relapse with a dismal prognosis.[6]

As the latest overall survival analysis (22 March 2018) was based on immature data, with 61% of events, the EMA has requested that patients continue to be monitored for overall survival and yearly updates provided. The next analysis of overall survival is planned when data maturity is 70%.[6-8] It is possible that treatment effect at early data cut-offs may be overestimated.

Overall survival data may be confounded by anti-cancer treatments given after discontinuation of study medication. At the latest analysis (22 March 2018) within the durvalumab and placebo groups 41% (195/476) and 54% (128/237) of patients had received subsequent disease-related anti-cancer therapy. Fewer patients in the durvalumab group, compared with placebo, received subsequent immunotherapy, (8.0% versus 22%, [most received nivolumab, 6.3% and 19%]) and radiotherapy (17% versus 24%), respectively. In the respective groups 27% and 30% had subsequent cytotoxic chemotherapy and 9.9% and 13% had targeted therapy.[8] The study has been unblinded and it is possible further overall survival analysis may be confounded by subsequent anti-cancer therapies.

The study population comprised 42% with PD-L1 ≥1%, 21% with PD-L1 <1% and 37% with unknown PD-L1 status, whereas the licensed indication is restricted to PD-L1 ≥1%. A post hoc analysis requested by the EMA indicated that in the subgroup with PD-L1 <1% durvalumab had a considerably lower effect on PFS and no effect on overall survival. The EMA concluded that patients with PD-L1 <1% should be excluded from the indication as efficacy could not be unequivocally established in this group. This was also supported by the mechanism of action of durvalumab.[6]

The PACIFIC study excluded patients who received sequential chemotherapy and radiotherapy, patients with poor performance status of at least 2 and patients with unresolved toxicity of at least grade 2 following chemoradiotherapy.[6] This may limit application of study results to these groups. Patients were excluded if they were not able to commence treatment within six weeks (two weeks before protocol amendment) after their last radiotherapy.[6] Only 25% (182/713) of patients commenced treatment less than two weeks after radiotherapy, with the majority, 75% (531/713), randomised to study treatment between two and six weeks after radiotherapy. The hazard ratios (HR) (95% confidence interval [CI]) for PFS and overall survival were 0.39 (0.26 to 0.58) and 0.42 (0.27 to 0.67), respectively, in patients starting treatment within two weeks of radiotherapy and were 0.63 (0.49 to 0.80) and 0.81 (0.62 to 1.06), respectively, in those that started treatment between two and six weeks after radiotherapy.[7,8] There are no data on the efficacy of durvalumab commenced more than six weeks after radiotherapy.

The EMA review noted that age is a prognostic factor in NSCLC. Mean age at diagnosis has risen over the last decades from 60 to 65 years to approximately 70 to 72 years in Caucasian patients, with most patients above 65 years at the time of diagnosis. It was noted that patients in the PACIFIC study were younger, mean age approximately 63 years and median age 64 years (range 23 to 90 years). The study included 55% of patients aged less than 65 years and 45% at least aged 65 years.[6]

Pre-specified subgroup analyses by a range of baseline demographic and disease characteristics were generally consistent with analyses of PFS and overall survival in the total study population. However, the EMA review noted that there seems to be a greater effect in younger patients (<65 years) compared with older patients (≥65 years). In the subgroup of older patients, aged at least 65 years the HR (95% CI) for PFS was 0.74 (0.54 to 1.01), while in the subgroup of younger patients, aged less than 65 years the HR (95% CI) for PFS was 0.43 (0.32 to 0.57).[6-8]

Clinical experts consulted by SMC consider durvalumab in maintenance treatment of stage III NSCLC to be a therapeutic advance due to effects on PFS and overall survival. They note that it would be used in practice in accordance with the product licence, that is, for patients with PD-L1 on ≥1% of tumour cells who do not have disease progression after platinum-based chemoradiotherapy.

The Scottish Pathology Network (SPAN) has advised that upfront PD-L1 testing is routine in many Scottish health boards. Therefore, the introduction of durvalumab for stage III NSCLC would be expected to have no impact on pathology services.

At the PACE meeting, it was noted that durvalumab would offer hope for patients to potentially delay or prevent further disease progression. It may increase the proportion of patients achieving disease control and increase overall survival. Available data are currently immature, but the PACE clinicians noted that durvalumab may offer the possibility of cure for a small number of patients. Durvalumab may also reduce the incidence of brain metastases which are common in lung cancer patients and have a substantial impact on the quality of life and independence of affected patients.

Patient and clinician engagement

A PACE meeting with patient group representatives and clinical specialists was held to consider the added value of durvalumab as an ultra-orphan in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- Locally advanced (stage III) NSCLC is a devastating diagnosis with a poor prognosis and a 5 year survival of 15 to 30%.
- Following chemoradiation therapy, patients are currently not given active treatment and there is an unmet need for effective treatments to improve the long-term survival of patients who, after chemoradiation, would currently only be under surveillance for signs of disease progression.
- PACE clinicians considered that durvalumab offered a major therapeutic advancement for the small group of patients with stage III NSCLC. It offers hope to potentially delay or prevent further disease progression. Available data are currently immature, but the PACE clinicians noted that durvalumab may offer a possible cure for a small number of patients.
- By delaying or preventing the progression to stage IV disease, durvalumab may reduce the need for future treatment and reduce overall toxicity for the patient. This may substantially improve the quality of life of patients, family and carers by allowing patients to continue with normal, working and family life and by relieving the psychological distress associated with stage III disease.
- Durvalumab is a tolerable treatment similar to other immunotherapy which clinicians have experience in managing. Patients are prepared to undergo 12 months of this additional treatment for the potential survival benefits.

Additional Patient and Carer Involvement

We received patient group submissions from the Roy Castle Lung Cancer Foundation and the Scottish Lung Cancer Nurses Forum. The Roy Castle Lung Cancer Foundation is a registered charity and the Scottish Lung Cancer Nurses Forum is an Unincorporated Organisation. The Roy Castle Lung Cancer Foundation has received 7.5% pharmaceutical company funding in the past two years, including from the submitting company. The Scottish Lung Cancer Nurses Forum has received 80% pharmaceutical company funding in the past two years, including from the submitting company. Representatives from both organisations participated in the PACE meeting. The key points of their submissions have been included in the full PACE statement considered by SMC.

Value for money

The company submitted a cost utility analysis comparing durvalumab plus standard of care (SoC) to SoC alone for the treatment of patients with locally advanced, unresectable, stage III NSCLC whose tumours express PD-L1 on ≥1% of tumour cells and whose disease has not progressed following platinum-based chemoradiation therapy. SoC was assumed to consist of active follow up, followed by subsequent post progression therapies, which included

further PD-L1 treatments. Based on SMC expert responses, SoC is an appropriate comparator.

A three state semi Markov model was submitted over a 40 year time horizon, which consisted of a progression free health state, post progression health state and death. The model uses PFS, time to progression and post progression data in conjunction with parametric functions, to estimate the proportion of patients in each health state over time. The clinical data used in the economic analysis were derived from the PD-L1 ≥1% subgroup in the PACIFIC study. Efficacy for SoC was based on the placebo arm within this study.[6]

The model estimates PFS for both durvalumab and SoC arms based on patient level Kaplan Meier data (using the latest data cut, March 2018). A generalised gamma curve was fitted to these data to extrapolate the proportion of patients remaining progression free over time. For post progression survival, data from the durvalumab and placebo arms of PD-L1 ≥1% subgroup were pooled, that is the model assumes no difference in post progression survival between treatment arms. An exponential function was fitted to the pooled Kaplan Meier data to extrapolate post progression survival. The model incorporates a waning in treatment effect, which was applied to the durvalumab arm after 5 years, such that durvalumab was assumed to have the same efficacy as SoC for the remainder of the model time horizon. Durvalumab resulted in a median modelled overall survival benefit of 58 months compared to 28.5 months for SoC.

Medicine acquisition costs were included as well as administration costs. The base case analysis assumed vial sharing occurs with durvalumab 50% of the time. Within the economic analysis durvalumab treatment costs were estimated based on the average patient weight in the PACIFIC PD-L1 ≥1% population (71.1kg). Costs were modelled using time to treatment discontinuation. Other costs included monitoring costs associated with disease management in each health state, end of life costs and adverse event costs, which were applied to both treatment arms. Resource use estimates were based on clinical opinion, ESMO guidelines and published technology appraisals.[10,11] Patients who experienced disease progression received subsequent treatment costs. SMC experts noted that patients in practice are unlikely to receive further PD-L1 treatment, therefore the company's decision to include these treatments may be seen as conservative. The cost associated with PD-L1 testing was included in the model. The model assumes that all patients eligible for durvalumab will require testing.

Utility values were derived using the EQ-5D-5L. These data were collected from the PACIFIC study and mapped to EQ-5D-3L using a published mapping function.[12] Within the model, disease progression was considered to be the primary impact on quality of life. The utility value for the progression free and progressed health states were estimated to be 0.81 and

0.776 respectively. Disutilities associated with adverse events were also included in the analysis.

A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. SMC would wish to present the with-PAS cost-effectiveness estimates that informed the SMC decision. However, owing to the commercial in confidence concerns regarding the PAS, SMC is unable to publish these results. As such, only the list price figures can be presented.

The base case results and key sensitivity analyses results are presented in tables 2 and 3 below. Durvalumab resulted in an incremental life year gain and a quality adjusted life year (QALY) gain versus SoC, as a higher proportion of patients remained in the progression free health state. Incremental costs were primarily due to the treatment costs associated with durvalumab.

Table 2: Base case results (list price)

Treatment	Incremental costs	Incremental QALYs	Incremental cost effectiveness ratio (ICER)
SoC	-	-	-
Durvalumab	£60,255	2.35	£25,629

Table 3: Key scenario analyses results (list price)

Scenario analysis	Incremental costs	Incremental QALYs	ICER
Time horizon (10 years)	£59,663	1.34	£44,533
Time horizon (20 years)	£60,125	2.05	£29,390
Progression free survival modelled using a log normal curve	£63,084	1.39	£45,448
Utility values for progression free and progressed disease 0.60 and 0.38 respectively	£60,255	1.82	£33,176
Subsequent treatments (alternative post progression survival curve used + 50% subsequent immuno-oncology after SoC use)	£58,350	1.93	£30,197
Utility values incorporating progression and time to death	£60,255	2.36	£25,514
No vial sharing	£62,151	2.35	£26,435

Combined scenario analysis whereby the time horizon is reduced to 20 years, log normal curve applied to Kaplan Meier PFS data in both treatment arms and a 10% utility decrement is applied to the progression free and progressed disease health states	£64,959	1.20	£54,168

QALY=quality-adjusted life year, ICER= incremental cost-effectiveness ratio

There were a number of limitations with the analysis which were as follows:

- A generalised gamma curve was used extrapolate PFS and was fitted to both the placebo and durvalumab treatment Kaplan Meier data. The generalised gamma was considered to be the best fit to the data based on goodness of fit statistics and seems to provide a reasonable fit to both treatment arms up to 18 months based on visual inspection. However, given the low numbers of patients at risk post 18 months, the generalized gamma may not accurately reflect longer term clinical data and when compared to other curves, it appears to provide the most favorable PFS estimates for durvalumab. Based on comments from the SMC statistical advisor, an alternative curve, such as the lognormal could be considered a reasonable fit. The use of the lognormal curve in a scenario analysis has a considerable upward effect on the ICER.
- Given the mean age of diagnosis and nature of the condition, the base case time horizon may not be appropriate. A 20 year time horizon appears to be long enough to adequately capture the differences in costs and benefits between the two treatment arms. Previously published NICE and SMC health technology appraisals for NSCLC have incorporated 20 year time horizons within their base case analysis.
- The utility values for progression free and progressed disease appear relatively high when compared to similar health states in previous health technology assessments for NSCLC. However, the disparity may be plausible given that previous appraisals have related to stage IV NSCLC, where patients are likely to have poorer quality of life. Furthermore, base case utility values were derived directly from patients within the PACIFIC study, which is considered appropriate. The ICER is sensitive to using lower values for these modelled health states.

Impact beyond direct health benefits and on specialist services

By prolonging disease-free survival, durvalumab may decrease the need for subsequent chemotherapy or immunotherapy, reducing overall toxicity and hospital treatment for the patient. Delayed progression may allow patients to remain well for longer, continue with normal working and family life and relieve the psychological distress associated with stage III

disease. This may lessen the overall burden of disease on patients and on their family and carers. Patients were prepared to make the extra hospital visits for durvalumab administration every 2 weeks for 12 months for the hope of improved patient survival. Since only a small number of patients would be eligible for durvalumab, the burden of this additional treatment on the service is expected to be small and clinicians have experience in the management of immunotherapy.

Costs to NHS and Personal Social Services

The company estimated there would be 75 patients eligible for treatment with durvalumab in year 1 increasing to 76 patients in year 5. The uptake rate was estimated to be 33.5% in year 1 (25 patients) rising to 90% in year 5 (69 patients).

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS.

The submitting company did not estimate any costs outside the NHS.

Conclusion

The Committee also considered the benefits of durvalumab in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that the criterion for a substantial improvement in life expectancy was satisfied. In addition, as durvalumab is an ultra-orphan medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence and the output from the PACE process, and after application of the appropriate SMC modifiers, the Committee accepted durvalumab for use in NHSScotland.

Additional information: guidelines and protocols

In 2017 the European Society of Medical Oncology (ESMO) published *Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO clinical practice guidelines for diagnosis, treatment and follow-up.* These recommend that concurrent chemoradiotherapy is the treatment of choice in patients with unresectable stage IIIA and IIIB NSCLC. If concurrent chemoradiotherapy is not possible for any reason sequential chemotherapy followed by definitive radiotherapy represents a valid and effective alternative. In the absence of

contraindications, the optimal chemotherapy to be combined with radiation in stage III NSCLC should be based on cisplatin. In the stage III disease chemoradiotherapy strategy, two to four cycles of concomitant chemotherapy should be delivered. There is no evidence for further induction or consolidation chemotherapy. In sequential approaches, radiotherapy delivered in a short overall treatment time is recommended. NSCLC patients treated with radical intent should be followed for treatment-related complications, detection of treatable relapse or occurrence of second primary lung cancer. Surveillance should be every six months for two years and then annually to detect second primary tumours.[2]

In February 2014 the Scottish Intercollegiate Guidelines Network (SIGN) issued publication number 137: *management of lung cancer*. This recommends concurrent chemoradiotherapy should be administered to patients with locally advanced NSCLC suitable for radical radiotherapy who have a good performance status (performance status 0-1). Treatment within a clinical trial is recommended as good practice.[3]

In April 2011 the National Institute for Health and Care Excellence (NICE) issued clinical guideline number 121: *lung cancer, diagnosis and management*. This recommends radical radiotherapy for patients with stage III NSCLC who have good performance status (WHO 0, 1) and whose disease can be encompassed in a radiotherapy treatment volume without undue risk of normal tissue damage. Chemoradiotherapy should be considered for patients with stage III NSCLC who are not suitable for surgery. Balance potential benefit in survival with the risk of additional toxicities.[4]

In October 2010 the British Thoracic Society (BTS) and the Society for Cardiothoracic Surgery in Great Britain and Ireland (SCS) published guideline on the radical management of patients with lung cancer. These recommend that chemoradiotherapy be offered to patients with locally advanced NSCLC and good performance status who are unsuitable for surgery. Selected patients with good performance status should be offered concurrent chemoradiotherapy with a cisplatin-based chemotherapy combination. Offer patients unsuitable for concurrent chemoradiotherapy sequential chemoradiotherapy.[5]

Additional information: comparators

There are no active comparators. Patients currently receive clinical follow-up with no maintenance therapy.

Cost of relevant comparators

Medicine	Dose Regimen	Cost per 1-year course (£)
Durvalumab	**10mg/kg IV every two weeks for up to one year**	**94,900**

Costs from British National Formulary based on a body weight of 70kg and calculated using the full cost of vials/ampoules assuming wastage. Costs do not take any patient access schemes into consideration.

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This assessment is based on data submitted by the applicant company up to and including 15 March 2019.

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews

and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.